said first baculovirus promoter and said second baculovirus promoter are two different promoters and are located at two different loci.

10) (Twice Amended) A method for preparing ~~an~~ immunoglobulin comprising the steps of:

infecting at least one insect cell with a recombinant baculovirus, said recombinant baculovirus comprising an expression vector comprising 1) a first expression cassette comprising a first sequence coding for at least one part of an immunoglobulin H chain, wherein said first sequence is under transcriptional control of a ~~second~~first baculovirus promoter and 2) a second expression cassette comprising a second sequence coding for at least part of an immunoglobin L chain, wherein said second sequence is under transcriptional control of a second baculovirus promoter, wherein said first baculovirus promoter and said second baculovirus promoter are two different promoters and are ~~lcated~~located at two different loci;

culturing ~~said~~ at least one insect cell in a culture medium~~; insect cells in accordance with Claim 9~~ and

extracting said immunoglobulin from the culture medium.

11) (Twice Amended) An immunoglobulin whose constant domain is coded by a sequence of human origin, obtained by the method of Claim 10.

Remarks

Applicants acknowledge with appreciation the Examiner's helpful suggestions concerning Claims 1, 10, and 11.

Claim 1 has been amended in accord with the Examiner's helpful suggestion, to insert "a" preceding the use of the terms " first expression cassette", and "second expression cassette."

We further note the Examiner's helpful suggestion regarding the vagueness of the recitation of the phrase, "culturing said at least one insect cell in culture medium; insect cells in accord with Claim 9", and as a result we have amended Claim 10. The amendment to Claim 10 also removes the antecedent basis issue regarding the term "second baculovirus promoter". In light of the foregoing, Applicants submit that the rejections of Claims 1-15 under 35 U.S.C §112, second paragraph are now obviated and the claims are now in proper form for allowance.

Turning now to the prior art rejection, Claim 11 has been rejected under 35 U.S.C §102 (b) as being anticipated by Paul et al. (U.S. Patent 5,229,272). Applicants have amended Claim 11, based on Claim 8 of the Applicants' original claims, to further define the human origin of the immunoglobulin obtained by the method taught in Claim 10.

We have no particular disagreements with the Examiner's helpful comments regarding the patentability of a product depending upon the method by which it is made. Applicants, however, respectfully submit that the immunoglobulin of Claim 11 demonstrates unexpected properties as compared to the immunoglobulin taught in Paul et al, and is thus patentable over the prior art. In *Ex parte Gray*, 10 U.S.P.Q.2d, 1992 (Bd. Pat. App. & Inter. 1989), the prior art disclosed a human nerve growth factor (b-NGF) isolated from human placental tissue, and the disputed claim was directed to b-NGF produced through genetic engineering techniques. In comparing the prior art to the claim, the Board found that the "factor" produced by both techniques was substantially the same, and thus obvious. In coming to this conclusion the Board stated that the dispositve issue is whether the claimed "factor" exhibits any unexpected properties compared to the "factor" disclosed by the prior art.

An immunoglobulin is constituted of the combination of two heavy chains (H) and two light chains (L). Each chain is then constituted of a variable region (VH and VL), which contain the antigen attachment site, and a constant region (CH and CL). The variable regions are the support of the specificity of the antibody for its antigen.

We invite the Examiner's attention to amended Claim 11 which recites an immunoglobulin whose constant domain is coded by a sequence of human origin. Thus, the immunoglobulin obtained by the method of Claim 10 is different from the immunoglobulin disclosed in Paul. The claimed immunoglobulin also has unexpected properties compared to the immunoglobulin disclosed by Paul.

Paul discloses components of antibodies which enhance the rate of chemical reaction. These components are catalytic and include a Fab portion of an antibody, the Fv portion of an antibody, a light chain, a heavy chain, a mixture of the unassociated light and heavy chains, dimers formed of the various combinations of light and heavy chains, a variable fragment of a light chain, a variable fragment of a heavy chain, a catalytic domain of a light chain and a catalytic domain of a heavy chain.

These components can be obtained in a number of different ways as disclosed at Column 3, lines 28 to 42 of Paul. These components may be purified from natural antibodies or sequenced and expressed by recombinant methods well known in the art as disclosed at Column 12, lines 30 to 56 of Paul.

However, none of these methods disclose the use of transformed cells from insects to express the components. Moreover, as explained in the enclosed abstract "Microheterogeneity of the Oligosaccharides carried by the N-glycosylation sites of the bovine lactotransferrin expressed in Mamestra brassicae using a baculovirus vector" from Lopez et al. (1997, Glycobiology 7: 635-651), the baculovirus/insect cell expression produces glycoproteins with a glycosylation pattern distribution identical to the natural glycoproteins but whose glycans are different as the ones found in the natural glycoproteins. As a consequence, an immunoglobulin produced by the baculovirus/insect cell expression system will be chemically different from the corresponding natural

immunoglobulin.

Also, Paul only teaches rodent or *non*-human based immunoglobulins. The Applicants have invented an immunoglobulin derived mostly of human origin to answer a long felt need in the art. It is well known in the art that rodent and non-human immunoglobulins have had limited therapeutic value for humans, because they tend to induce an undesirable human response. The limited therapeutic value of rodent and non-human immunoglobulins demonstrates that human immunoglobulins have unexpected properties as compared to rodent and non-human immunoglobulins. Following the principals articulated in *Ex parte Gray*, it is clear that the Applicants have demonstrated an immunoglobulin with unexpected properties. As a result, Applicants believe that Claim 11, as amended, now stands patentable over Paul et al.

In light of the foregoing, we believe the application is now in condition for allowance, which action is respectfully requested.

Respectfully submitted,

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